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Identification of resilient sows in Porcine Reproductive and Respiratory Syndrome virus infected farms[1]

Glòria. Abella[*], Elena Novell[*†], Vicenç Tarancon[†], Luis Varona[‡], Ramona N Pena*, Joan Estany*, Lorenzo Fraile*[2]

*****Departament de Ciència Animal, University of Lleida-Agrotecnio Center, Lleida, Spain.

† Grup de Saneajament Porcí, Lleida, Spain

‡ Instituto Agroalimentario de Aragón (IA2). Universidad de Zaragoza, 50013. Zaragoza, Spain

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[2]Corresponding author: lorenzo.fraile@ca.udl.cat

ABSTRACT:

The identification of resilient sows can improve reproductive performance in farms exposed to multiple challenges. A common challenge is the porcine reproductive and respiratory syndrome virus (PRRSV). A key issue to deal with disease resilience is to set up a feasible phenotyping strategy. Our aim was to develop a phenotyping criterion to discriminate susceptible from resilient sows in PRRSV-infected farms. A total of 517 Landrace x Large White gilts were classified as resilient (R) or susceptible (S) to PRRSV virus, following vaccination with MLV-PRRSV at 6-7 wk of age, in a PRRSV negative multiplication farm. Female piglets were phenotyped as R if their serum was negative to PRRSV at 7 and 21 d post-vaccination (DPV) or as S if their serum was positive at 7 and/or 21 DPV. Amongst them, 382 gilts were transferred to a PRRSV-positive production farm, where the number of piglets born alive (NBA), stillborn (NSB), mummified (NMU), lost (NLP=NSB+NMU) and total born (NTB = NBA+NLP) were recorded for almost three years. Data were collected during two periods according to the PRRSV farm health status, which were confirmed as either PRRSV-positive stable (endemic) or inestable (epidemic). Analyses were carried out under a Bayesian approach. The heritability for the resilience criterion was estimated using a threshold model. A linear (for NTB and NBA) and a binomial model (for NSB, NMU and NLP) on the resilience criterion by the farm health status were used to assess the difference between R and S sows. The heritability of the resilience criterion was 0.46 (SD 0.06). The probability of a piglet being lost was greater (≥0.97) in S than in R litters, regardless of whether the delivery occurred during a PRRSV outbreak (20.5% vs 17.0%) or not (15.8% vs 13.7%). The lower piglet mortality rate in R sows was due to NSB, in the endemic phase (13.0% vs 15.0% of NTB, with a posterior probability of 98% of S sows showing higher NSB than R sows), and to NMU, in the epidemic phase

(4.0% vs 8.4% of NTB, with a posterior probability of >99% of S sows showing higher NMU than R sows). During a PRRSV outbreak, the S sows were twice as likely to give birth to a mummified piglet as compared to R sows. These findings provide evidence that the described phenotyping scheme has a potential use as a PRRSV resilience criterion.

Key words: PRRSV, resilience, phenotyping method, sow

INTRODUCTION

Reproduction is influenced by a number of infectious and non-infectious factors (environment, nutrition and management), which makes reproductive outcome a multifactorial process. A resilient sow is an animal that is able to maintain reproductive performance while facing different on-farm challenges. A frequent challenge is the infection with the porcine reproductive and respiratory syndrome virus (PRRSV) due to its high prevalence in intensive pig production areas (Fraile et al., 2010). This infection causes the largest economically significant disease impacting commercial pig production in North America, Europe, and Asia (Nathues et al., 2017). In sows, PRRSV can cause late-term abortions, prolonged anoestrus, an increase in stillborn and mummified piglets, coughing and respiratory problems whereas respiratory symptoms and reduced growth performance are frequently observed in young pigs (Lunney et al., 2010).

Epidemiological models applied to viral infections have demonstrated that selection for resilience should reduce both the likelihood and the impact of epidemics (Doeschl-Wilson and Kyriazakis, 2012). Key steps in the development of selection

programs for disease resilience include identification of resilient phenotypes, which involves resistance and/or tolerance to the pathogen, and characterization of its genetic variation. A body of evidence associates host genetics with different outcomes following PRRSV infection in the respiratory form of the disease (Petry et al., 2005; Reiner et al., 2010; Boddicker et al., 2014[ab]; Hess et al., 2016; Reiner, 2016). Moreover, it has also been described that there is a great variation in the reproductive performance among sows in response to PRRSV infection, thereby suggesting that this trait could respond to selection (Rashidi et al., 2014; Serao et al., 2014; Harding et al., 2017). Thus, the goal of this research was to set up a feasible phenotyping strategy to identify resilient sows in PRRSV endemic infected farms and then to assess how much of the variation can be attributed to their genetic background.

MATERIALS AND METHODS

All experimental procedures were approved by the Ethics Committee for Animal Experimentation of the University of Lleida and performed in accordance with authorization 7700 issued by the Catalan Department of Agriculture, Livestock, Fisheries and Food (Section of biodiversity and hunting).

Farms

One PRRSV-negative multiplication farm of 350 Landrace sows and one PRRSV-positive production farm of 1500 Landrace x Large White sows were included in this study. Both farms worked with weekly farrowing batches in all-in/all-out management system and they belonged to a large integration Spanish company (Pinsos del Segre S.A, Lleida, Spain). The multiplication and production sow farm were a farrow-to-finish

and farrow-to-wean farm, respectively. Animals of both farms were never commingled with piglets of other pig production flows. The routine vaccination program included sow immunization against swine parvovirus, Aujeszky disease virus, swine influenza virus, *Erysipelotrix rhusiopathie*, *Escherichia coli* and *Clostridium perfringens* in both farms. Furthermore, piglets were vaccinated against *Mycoplasma hyopneumoniae* (Mhyo) and porcine circovirus type 2 (PCV2) at weaning (three weeks of age). A PRRSV modified live vaccine was never used either in the multiplication or in the production farm during the study period. No signs of any major pig disease, with the exception of PRRSV during an outbreak period in the production farm, were present during the experiment.

Monitoring of PRRSV health status of farms

PRRSV health status for both farms was monitorized throughout the trial following previously published recommendations (Holtkamp et al., 2011). Briefly, herd classification for PRRSV was based on determining both shedding and exposure status of the herd. Testing methods to determine shedding and exposure to this virus include its direct detection by quantitative reverse transcriptase PCR (qRT-PCR) and antibody testing, respectively (details of the techniques are provided below). Classification was established by monitoring the PRRSV status of specific subpopulations in a herd. In our case, the relevant subpopulations were adult breeding animals, weaning-age pigs, breeding replacement animals and, growing pigs (24 weeks of age). Testing was based upon monthly sampling of 30 and 60 serum samples for shedding and exposure, respectively, from each animal subpopulation (Holtkamp et al., 2011). This sampling strategy allows detecting the presence of the virus with prevalence equal or higher than 10% and with a confidence level of 95%. In the case of weaning-age pigs, serum

samples from runt piglets were intentionally selected to increase the sensitivity to detect PRRSV.

The PRRS virus shedding status was classified as negative or positive. A negative shedding status meant that all the serum samples tested by qRT-PCR were negative (absence of viral shedding in the herd) while a positive shedding status meant that at least one serum sample tested positive by qRT-PCR (evidence of viral shedding and transmission in the herd). The exposure status was also classified as negative or positive. A negative exposure status meant there was absence of antibodies to the virus in the samples tested. On the contrary, a positive exposure meant that there was presence of antibodies to the virus.

Finally, the health status of the farm was considered endemic (EN) or epidemic (EP) according to the absence or presence of overt reproductive problems in the sow farm, respectively. This overt reproductive problems (epidemic situation) were based on a significant increase of abortions and/or lost piglets (stillborns and mummified) versus the baseline situation (endemic situation) in the sow farm.

Phenotyping for PRRSV resilience

At birth, 517 Landrace x Large White female piglets from 116 litters born in the multiplication farm were ear-tagged with their dam´s number in four non-consecutive biweekly batches during twelve months. Litters were produced by randomly mating available sows with 16 boars using monospermic artificial insemination, although the boar which sired a given litter was not annotated. The same sires were used across the experiment and only 7 dams produced gilts in two different batches. Crossfostering was not allowed for the sows included in the trial. Piglets were classified as resilient (R) or susceptible (S) to PRRSV virus according to the outcome of a vaccination with a

PRRSV modified live vaccine (MLV-PRRSV - Porcilis PRRS® MSD Animal Health) as follows. They were vaccinated at 6-7 wk of age following manufacture´s recommendations (2 mL by intramuscular dose that is equivalent to 10^5 $TCID_{50}$ of PRRSV DV strain by animal). Blood samples were drawn at 0, 7, 21, and 42 d post-vaccination (DPV) and collected in tubes (Vacutainer®, Betson Dickinson Ltd) in order to obtain serum. The vaccination procedure was carried out in a facility out of the multiplication farm to avoid transmission of the PRRSV vaccine strain to the sow farm. In the samples drawn at 0, 7, and 21 DPV, PRRSV viraemia was determined using a semi-quantitative TaqMan PCR. The PCR was performed as a routine diagnostic test by personnel of the Group of Sanejament Porcí (Group of Sanejament Porcí, Lleida, Spain). Thus, total RNA was isolated from serum using a MagMAX-96 Viral RNA Isolation Kit (Applied Biosystems, Foster City, CA) in accordance with the manufacturer's instructions. The PCR master mixes were obtained from the AgPath ID NA & EU PRRSV kit (Applied Biosystems) and assays were set up as a 1-step RT-PCR reaction, according to kit instructions. The RT-PCR reactions were carried out on a QST 7500 Real-Time PCR System (Applied Biosystems) in a 96-well format according to the manufacturer's recommendations. The assay results were reported as positive or negative depending on the cycle threshold (Ct) value ($Ct<40$ is positive). Finally, the sample collected at 42 DPV was used in this same laboratory to determine the PRRSV antibody titer (sample-to-positive ratio) by ELISA (IDEXX PRRS X3, IDEXX laboratories Inc, Westbrook, Maine, USA). In line with previous results in Abella et al., (2016), a piglet was phenotyped as R if its serum was negative to PRRSV according to the PCR outcome at 7 and 21 DPV. On the contrary, a piglet was classified as S if any of its samples at 7 and/or 21 DPV was positive.

Litter size recording

After being phenotyped as R or S, 382 females from 110 litters were subsequently transferred to the production farm following the standard operations procedures in course at the company. These females were those available at 7 mo of age (130 kg BW, SD 15) after natural mortality during fattening and regular culling for lameness, leg conformation, number of functional teats and other causes such as umbilical or inguinal hernias. On arrival, the gilts were allocated first in the quarantine unit of the production farm, where they were vaccinated against swine parvovirus, Aujeszky disease virus, swine influenza virus, *Erysipelotrix rhusiopathie*, PCV2 and Mhyo. Once in the reproduction unit, they were artificially inseminated to meet weekly production goals. Sows were culled if they returned to estrus more than twice, suffered chronic lameness, rectal or vaginal prolapse, or showed a body condition lower than 2 (in a scale from 1 to 4). Farm staff was not aware of which phenotype (R or S) the sows had throughout the whole experiment. Then, the farrowing date and the number of piglets born alive (NBA), stillborn (NSB) and mummified (NMU) per litter were recorded for almost three years (2016-2018). The total number of lost piglets per litter (NLP) was calculated as the sum of NSB and NMU. Combining NSB and NMU into a single trait was carried out to preclude misdiagnosis between them, which cannot be rule out in non-experimental farm recording schemes. Finally, the total number of piglets born per litter (NTB) was calculated summing up NBA and NLP. All sows produced at least one litter. The description of the litter size data used in this experiment is given in Table 1.

Statistical analysis

Inferences were based on Bayesian models. The heritability for the resilience criterion (R, S) was estimated using a liability threshold (probit) model (Sorensen and Gianola, 2002), which assumes an underlying normal distributed liability that, over a given threshold, produces a positive outcome. The liability was explained by a linear model including as explanatory factors the vaccination batch (4 batches) and the additive genetic effect of the pig (519 levels). Flat priors bounded at a very large value (M) were used for the batch (-M, M) and the additive genetic variance (0, M) while the residual variance was set to unity. The additive genetic effects, conditional on the additive genetic variance, were assumed multivariate normally distributed with mean 0 and with the numerator relationship (co)variance matrix calculated with a pedigree of 517 pigs from 116 full-sib families. The heritability for viral load and for antibody titer was estimated using the same linear model as for the liability of the resilience criterion. This model, with the resilience criterion added as a new systematic factor, was used to estimate the difference between S and R sows for antibody response.

The effect of the resilience criterion on NTB and NBA, both assumed normally distributed, was assessed using a lineal model including the vaccination batch (4 batches), the parity (from 1 to 7) and the resilience (R, S) by farm health status (EN, EP) at the time of farrowing (4 levels) as systematic factors and the sow (382 levels) and the full-sib family (110 levels). The NSB, NMU and NLP were analyzed assuming the following binomial distribution (Varona y Sorensen, 2010):

$$f(\mathbf{y}|\mathbf{t},\boldsymbol{\phi}) = \prod_{i=1}^{n} \binom{t_i}{y_i} \phi_i^{y_i} (1-\phi_i)^{t_i - y_i}$$

where y, t and $\boldsymbol{\phi}$ are, respectively, the vectors of n data (NSB, NMU or NLP), NTB, and probabilities to be stillborn (for NSB), mummified (for NMU), or lost (for NLP). At the next level of hierarchy, the logit transformation of $\boldsymbol{\phi}$ in litter *i* was described as for NTB and NBA but adding a quadratic polynomial on NTB as covariates. The individual

effects of the sow and the full-sib family were assumed to follow a normal distribution of mean 0 and variance σ_s^2 and σ_f^2, respectively. As above, flat priors bounded at very large values were used for systematic effects, covariates and variance components. Marginal posterior distributions for all unknowns were estimated using Gibbs sampling (Gelfand and Smith, 1990). Statistical inferences (namely, posterior standard deviations (PSD), posterior probabilities of S-R being greater than 0 (P_0), and highest posterior density intervals at 95% of probability [HPD95]) were derived from the samples of the marginal posterior distribution using a unique chain of at least 1,000,000 iterations, where the first 200,000 were discarded and 1 sample out of 100 iterations was retained. Models were solved using own software.

RESULTS

Variability and heritability for the resilience criterion

The PRRSV was never detected by PCR in the serum of 184 out of 517 female piglets (35.6%) after vaccination with a MLV-PRRSV vaccine. These percentages were comparable across batches (from 30.2% to 48.1%). In contrast, the virus was detected at 7 DPV (217 piglets) and/or 21 DPV (116 piglets) in 64.4% of the animals. Mean Ct in positive piglets at 7 DPV was 31.1 (SD 3.7) and mean PRRSV antibody titer at 42 DPV was 2.06 (SD 0.78). Differences among batches were very small, ranging from 30.5 to 31.7, for viral load, and from 1.86 to 2.27, for antibody titer. The results indicated that there is evidence of genetic variation associated with the R/S criterion. The posterior mean of the additive genetic variance at the level of the liability was 0.89 (PSD 0.23). As a result, the posterior mean of the heritability for the resilience criterion was 0.46 (PSD 0.06), with a posterior probability of 95% of being at least 0.36. These values

were in line with the estimates of the heritability for viral load in positive samples at 7 DPV (0.47, PSD 0.11) and for antibody titer at 42 DPV (0.69, PSD 0.10). The resilience criterion presented a positive relationship with antibody response. In particular, the S gilts had a higher antibody titer at 42 d (+0.85, P_0>0.99) than the R gilts.

Resilience criterion and litter size

The effect of the resilience status of a sow on litter size and piglet losses by the farm health status is given in Table 3. The percentage of sows of each phenotype with reproductive data (136 R and 246 S) was in line with the observed in challenged piglets, thereby indicating that previous culling policies were independent from the resilience criterion. There is evidence that the S sows had more NTB than the R sows, both in the EN (+0.44 piglets, P_0 = 0.94) and in the EP (+0.74 piglets, P_0= 0.92) scenario. No relevant difference between resilience statuses was observed for NBA, although their relative values relied upon the farm health status, with the S sows having more NBA in the EN phase (+0.20 piglets, P_0=0.79), but less in the EP phase (-0.15 piglets, P_0=0.38). This reversal trend can be explained by the higher mortality at birth in the deliveries from S sows as compared to R sows. In fact, even adjusting for litter size, the probability of a piglet being lost is greater (P_0>0.97) in S than in R litters, regardless of whether the delivery occurred during a PRRSV outbreak (20.53% vs 16.97%) or not (15.78% vs 13.70%). Interestingly, the origin of the decreased mortality in R litters differed according to the disease phase. Thus, while in the endemic situation the decline in piglet mortality rate in R sows was due to decreased NSB (12.98% vs 14.95% of NTB, with S sows showing higher proportion of NSB than R sows, P_0=0.98), in the epidemic situation it was to less NMU (4.00% vs 8.40% of NTB, with S sows showing

higher NMU than R sows, P_0>0.99). In the PRRSV outbreak, the S sows were twice as likely to give birth to a mummified piglet as compared to R sows.

DISCUSSION

All the samples obtained in the multiplication farm were negative either by PCR (shedding status) or antibody detection (exposure to the virus) throughout the trial. According to the classification proposed by Holtkamp et al., (2011), this farm was classified as PRRSV negative. As expected, all samples tested before vaccination (day 0 of the trial) were negative. This result is critical because it ensures that only naïve animals were vaccinated with the PRRSV MLV vaccine.

The PRRSV health status of the production farm changed through time, from EN to EP according to the qRT-PCR test described above. Thus, samples from adult breeding animals, weaning-age pigs, and breeding replacement animals were negative by PCR (shedding status) during the EN phase (from March 2016 to June 2018) and positive every month during the EP phase (from July to October 2018). On the other hand, most of the tested sera in both phases were positive for PRRSV antibody in adult breeding animals, weaning-age pigs, breeding replacement animals and growing pigs. The prevalence of PRRSV by antibody detection was equal or higher than 80% throughout the trial. During the EN phase, since no clinical signs (increase in abortion rate, early farrowing and sudden increase in NLP) compatible with a PRRSV outbreak were observed, the farm was classified as PRRSV positive stable (Holkamp et al., 2011), which means that PRRSV was endemically circulating. In contrast, in the EP phase, a sudden increase of NLP (Table 1) and early farrows (data not shown) were observed in line with a PRRSV outbreak and therefore during this phase the farm was classified as PRRSV positive non-stable farm.

296 The observed variability in response to vaccination is consistent with previous
297 results of our group, where 55.0% of the pigs were positive (Abella et al., 2016), and
298 with findings from pigs challenged with wild-type North American strains, where a high
299 variability of viral load after virus exposure was also observed (Boddicker et al.,
300 2014[ab]). Nevertheless, these last studies, unlike ours, which were based on a PRRSV
301 MLV of low virulence, used a high virulent PRRSV field strain. This is a relevant
302 difference that could explain why the pigs challenged with wild-type North American
303 strains were all positive whereas we were not able to detect the PRRS virus in around
304 35-45% of the challenged animals. Still, PRRSV antibodies were detected in serum at
305 42 DPV, clearly indicating that pigs were infected, although probably, for those scored
306 as negative, with a serum viral load below the detection threshold. Altogether, these
307 results reinforced the hipothesis that there exists variability in the response to PRRSV
308 infection in growing pigs, both to American and to European PRRSV strains (Petry et
309 al., 2005; Reiner et al., 2010; Islam et al., 2013; Reiner, 2016; Hess et al., 2016).

310 We set that a challenged piglet was resilient if its serum was negative to PRRSV
311 at 7 and 21 DPV and susceptible if any of the two samples was positive. In doing so, we
312 were assuming that a piglet phenotyped as resilient is able to control PRRSV replication
313 at early stages of infection, where innate immunity is playing a major role (Loving et
314 al., 2015). The novelty of our approach relies on linking the response to PRRSV
315 exposure at a very early age of the rearing period with their future reproductive outcome
316 in PRRSV-positive farms. As confimed by accepted diagnostic procedures (Holtkamp et
317 al., 2011), the reproductive outcome of the gilts in this study was recorded in a farm
318 which succesively was PRRSV-positive stable (for 27 months) and PRRSV-positive
319 unstable (for 4 months). With the previous hypothesis in mind, we were able to
320 associate the resilient phenotype R with lower piglet mortality, both in PRRSV non-

outbreak and outbreak disease situations. This agrees with previous observational (Rashidi et al., 2014; Serao et al., 2014) and experimental studies (Ladining et al., 2014) with American PRRSV-infected gilts and sows, where the extension of the disease in fetuses was highly variable both between and often within litters. Our findings confimed that a negative response of naïve gilts to PRRSV vaccination with MLV-vaccine affects their lifelong piglet mortality in PRRSV-infected farms. The reproductive performance of a sow depends on infectious and non-infectious factors. Since the gilts in our study were allocated in a conventional PRRSV-positive farm, they were exposed to PRRSV but potentially to many other pathogens. Thus, their reproductive outcome is the result of their intrinsic reproductive capacity in a PRRSV-free enviroment plus their resilience to PRRSV and other diseases such as PCV2 infection among others. In this trial, these three components cannot be disentagled because each individual pathogen burden is not known. However, since R and S gilts were randomly allocated in contemporary production batches, they had the same probability to get infected with PRRSV or any other pathogen affecting reproduction. Therefore, the lack of individual diagnosis does not add any bias to our study.

There is evidence that the individual genetic background is involved in the reproductive consequences of PRRSV disease. In this line, Lowe et al., (2005) concluded that genetics influenced abortion rates in PRRSV-infected sows and Lewis et al., (2009b), in an extensive study, that there is a great inter-breed variation for reproductive performance in PRRSV outbreaks. The resilience criterion described here could be a first step to take advantage of this variability within a given population. We cannot discard the effects of other diseases on reproduction and therefore our criterion cannot be claimed as disease-specific, but, due to the clinical history of the farm, PRRSV is likely the main driver of its association with piglet mortality. Moreover, the

346 results obtained, indicating that the largest difference between R and S sows was for
347 NMU during the PRRSV outbreak would confirm this hipothesis since increased NMU
348 is likely the most identifiable clinical outcome in an acute PRRSV outbreak in sows.

349 The genetic mechanisms involved in disease-resilience are not yet fully
350 characterized, but it is well known that the genetic variation underlying innate resistance
351 and acquired immunity is polygenic (Harding et al., 2017). The value of the estimate of
352 the heritability for our resilience criterion indicates that the polygenic background
353 explains around half of the observed variation. This estimate, given that it is only based
354 on a full-sib design, is likely overestimated due to potential maternal or common litter
355 effects. As a counterpart, some underestimation is also expected, provided that all litters
356 were assumed to be produced by different sires when they are not (van der Werf and
357 Thompson, 1992). Even with these limitations, results show that there is scope to
358 improve resilience through selection and appropriate management. The use of field data
359 to estimate the heritability of resilience-traits has been addressed previously, and pros
360 and cons revised in detail (Bishop et al., 2010; Bishop et al., 2012). It has been
361 demonstrated that the heritability of NLP increases during PRRSV outbreaks (Lewis et
362 al., 2009[a]), thus confirming that there exists genetic variation for host resilience. In pigs,
363 a very high heritability ($0.45<h^2<0.81$) has been reported for immunological traits
364 associated with innate and adaptive immune responses (Clapperton et al., 2009; Flori et
365 al., 2011[ab]). In particular, following a PRRSV outbreak in a naïve farm, Serao et al.,
366 (2014) reported a high heritability (0.45) for antibody response to PRRSV (antibody
367 titer at 46 d post-infection) and, although the phenotypic correlation was almost null, a
368 high genetic correlation of the antibody response with NBA (0.73) and NSB (-0.72).
369 These results suggest that PRRSV antibody titer could be used as a proxy of the impact
370 of PRRSV on reproductive traits. In our study we also found a high heritability for the

antibody response but we were only able to detect a small but positive correlation of antibody response with NSB, as reflected by the higher antibody titer observed in S as compared to R piglets. However, it must be taken into account that we measured the antibody titer in growing animals (6-7 wk of age) after vaccination, whereas Serao et al., (2014) did it in pregnant sows after infection. More studies are needed to decipher the role of antibody production following a PRRSV infection as a resilience criterion in sows.

The high variability and ability described for the PRRSV virus for immune evasion makes it extremely difficult to design effective vaccines, especially under heterologous situations (Nan et al., 2017). Thus, tools other than vaccination are urgently needed to control this disease. Among them, the use of more resilient pigs could be an option. Resilient pigs will probably show less clinical signs and shed fewer viruses after PRRSV infection (Rowland et al., 2012). As a result, the infection pressure within and between herds could be substantially reduced, with subsequent improvement in health and productive performance (Reiner, 2016). To our knowledge, this is the first time in the literature that a practical phenotyping criterion for PRRSV resilience is experimentally contrasted under field conditions. Interestingly, the PRRSV strain used for vaccination was different from the strain found in the production farm (only 85% of similarity). The fact that even with a different strain we get response makes us believe that the resilient phenotypes are not strain-specific, thereby confirming the hypothesis that the proposed phenotyping procedure is targeting the innate rather than the acquired immune response.

Altogether, the results obtained indicate that the sows phenotyped as resilient are more efficient in environments where PRRSV is circulating, since they are able to cope with the same number of viable offspring than susceptible sows but at a lower

biological cost (i.e. lower NLP). All of this without considering that the piglets from resilient sows will likely develop also better at weaning and throughout the growing period. Conversely, we can put the question the other way around and ask whether susceptible sows, which produce larger litters (i.e. NTB), will perform better than R sows in PRRSV-negative farms. In this regard, it would be interesting to check whether the resilience criterion developed here is capturing a genotype by environment interaction effect, in the sense that the sows that are less sensitive to unfavorable conditions are also less productive in favorable environments. The promising results found in this study concerning piglet mortality reduction in PRRSV-positive farms should be confirmed in larger trials and validated in pigs infected with different PRRSV strains.

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559 **Table 1.** Description of litter size data used in the analyses by farm health status

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	Farm health status					
	Endemic			Epidemic		
Trait[1]	No. of litters	Mean	SD	No. of litters	Mean	SD
NTB	1280	13.5	3.7	184	15.2	3.8
NBA	1280	11.7	3.3	184	11.7	3.5
NSB	1280	1.7	2.0	184	2.5	2.3
NMU	1280	0.1	0.4	184	1.0	1.7
NLP	1280	1.8	2.1	184	3.4	3.0

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562 [1] Number of piglets born alive (NBA), stillborn (NSB) and mummified (NMU) per
563 farrowing. The total number of lost piglets (NLP) was calculated as NSB plus NMU,
564 and the total number of piglets born per parity (NTB) as NBA plus NLP.

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566 **Table 2**. Posterior estimates for heritability distribution for PRRSV resilience criterion,
567 viral load and antibody titer
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Trait[1]	Mean	SD	Mode	HPD95[2]	k[3]
Resilience criterion	0.46	0.06	0.46	0.34 ; 0.59	0.36
Viral load	0.47	0.11	0.47	0.19 ; 0.75	0.24
Antibody titer	0.69	0.10	0.69	0.49 ; 0.90	0.52

570
571 [1] Resilience criterion, susceptible or resilient based on whether the PRRSV virus is
572 present or not in serum samples at 7 or 21 d post-vaccination; viral load, PCR cycle
573 threshold of positive serum samples at 7 d post-vaccination; antibody titer, sample-to-
574 positive ratio in serum samples at 42 d post-vaccination.
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576 [2]HPD95: highest posterior density interval at 95%.
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578 [3]k: limit for the interval [k, +∞] having a probability of 95%.
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Table 3. Expected number of total born (NTB), born alive (NBA) and the percentage of stillborn (ϕ_{NSB}), mummified (ϕ_{NMU}) or total losses (stillborn and mummified) (ϕ_{NLP}) versus NTB by farm PRRSV health (endemic or epidemic) and sow resilience status (R: Resilient; S: Susceptible).

	Farm health status					
	Endemic			Epidemic		
	Sow status			Sow status		
Trait	R	S	P_0[1]	R	S	P_0[1]
NTB	14.13	14.57	**0.94**	13.77	14.51	**0.92**
NBA	11.97	12.17	0.79	11.30	11.15	0.38
$\phi_{NSB, \%}$	12.98	14.95	**0.98**	13.26	13.63	0.59
$\Phi_{NMU, \%}$	0.65	0.72	0.63	4.00	8.40	**>0.99**
$\phi_{NLP, \%}$	13.70	15.78	**0.98**	16.97	20.53	**0.97**

[1] P_0: Posterior probability of S-R being positive. In bold, probabilities above 0.90.